

EXHIBIT 3

TREATMENT OF CANCER WITH NOVEL ANTI-IL13 MONOCLONAL ANTIBODIES

BACKGROUND

[0001] IL13 is a pleiotropic Th2 cytokine produced predominantly by CD4⁺ T-helper type 2 cells, as well as NKT cells, basophils, and mast cells (Hershey, GKK, *J Allergy Clin Immunol.* (2003) 111: 677-90). In addition to its etiologic roles in asthma, fibrosis, chronic pulmonary obstructive disease and ulcerative colitis (Wynn, TA, *Annu Rev Immunol.* (2003) 21: 425-56; Wynn TA., *Nat Rev Immunol.* (2004) 4: 583-94; Heller F et al., *Immunity* (2002) 17: 629-38), IL13 is also known to play important roles in tumor growth (Kapp U et al., *J Exp Med.* (1999) 189: 1939-4; Trieu Y et al., *Cancer Res.* 2004; 64: 3271-5) and modulation of tumor immunity (Terabe M et al., *Cancer Immunol Immunother.* 2004; 53: 79-85; Terabe M et al., *Nat Immunol.* 2000; 1: 515-20). Therefore, IL13 and its receptors are potential therapeutic targets for cancer.

[0002] Hodgkin's lymphoma (HL) is a malignant disorder of the lymph nodes characterized by the abnormal production of multiple cytokines from the malignant cell population of HL, the Reed-Sternberg (RS) cells (See Kapp et al. and Trieu et al., supra). IL13 was shown to promote HL proliferation by an autocrine mechanism. Anti-IL13 neutralizing monoclonal antibodies (MAbs) were shown to inhibit the proliferation of HL cells in vitro (Trieu et al. supra).

[0003] Accumulating evidence indicates that IL13 receptors are highly expressed on a variety of human malignant tumor cell lines (e.g., glioblastoma, head-and-neck tumors, squamous cell carcinoma, renal cell carcinoma, AIDS-associated Kaposi's carcinoma, prostate carcinoma, pancreatic carcinoma, and epithelial carcinomas such as adenocarcinoma of stomach, colon, and skin) (See e.g., Debinski W et al. *J Biol Chem.* (1995) 270: 16775-80; Puri RK et al. *Blood* (1996) 87: 4333-9; Maini A et al. *J Urol.* (1997) 158: 948-53; Debinski W et al. *Clin Cancer Res.* (1995) 1: 1253-8; Kornmann M et al. *Anticancer Res.* (1999) 19: 125-31; Husain SR et al. *Blood* (2000) 95: 3506-13; Kawakami K et al. *Cancer Res.* (2001) 61: 6194-6200). A recombinant fusion protein comprising IL13 coupled to a mutated form of *Pseudomonas* exotoxin was shown to specifically kill these tumor cells in vitro. Therefore, these data suggest that the IL13 receptor is an attractive target for directing selective tumor killing.

[0004] It is now known that the major mediators of anti-tumor immunity are CD4⁺ Th1 cells and CD8⁺ cytotoxic T lymphocytes (CTL). Since immune deviation toward Th2 suppresses Th1 development, it has been suggested that induction of a Th2 response in cancer patients is one of the major mechanisms repressing tumor immunosurveillance. Terabe et al. showed that an IL13 inhibitor (sIL13R α 2-Fc) inhibited tumor recurrence in a mouse model. Similar observations were also found with STAT6 or IL4R knockout mice, but not with IL4 knockout mice. Together, these results indicate that IL13 plays an important role in suppressing anti-tumor immunity in vivo. Therefore, inhibiting IL13 could promote anti-tumor immunity in cancer patients.

[0005] Antibody-based therapy has proved very effective in the treatment of various cancers. For example, HERCEPTIN® and RITUXAN® have been used successfully to treat breast cancer and non-Hodgkin's lymphoma, respectively. The present invention provides alternative